Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	31	Trono NEAR didier	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/21 09:55
L2	5169	(lentiviral lentivirus HIV$2) WITH vector	US-PGPUB; USPAT; EPO; JPO	OR	ON	2005/03/21 09:56
L3	7737	(replication NEAR (defective incompitant)) (self NEAR inactivating)	US-PGPUB; USPAT; EPO; JPO	OR	ON	2005/03/21 09:56
L4	1426	L2 and L3	US-PGPUB; USPAT; EPO; JPO	OR	ON	2005/03/21 09:56
L5	6569	hematopoietic ADJ stem ADJ cell	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/21 09:56
L6	62	L4 and (delet$5 NEAR LTR)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/21 09:56
L7	28	L6 and L5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/21 09:56
L8	2546	EF1$3 NEAR promoter (PGK NEAR promoter)	US-PGPUB; USPAT; EPO; JPO	OR	ON	2005/03/21 09:59
L9	179	L8 and L4	US-PGPUB; USPAT; EPO; JPO	OR	ON	2005/03/21 09:59
L10	67	L9 and L5	US-PGPUB; USPAT; EPO; JPO	OR	ON	2005/03/21 09:59
L11	15	L10 and SIN	US-PGPUB; USPAT; EPO; JPO	OR	ON	2005/03/21 09:59

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(FILE 'HOME' ENTERED AT 10:01:48 ON 21 MAR 2005)

FILE 'MEDLINE, CAPLUS, SCISEARCH' ENTERED AT 10:02:10 ON 21 MAR 2005
L1 93035 S HEMATOPOIETIC (L) (STEM OR PROGENITOR OR PRECURSOR) (L) CELL
L2 199 S (LENTIVIR? OR HIV(3W)VECTOR) (L) ((SELF(2W)INACTIVA?) OR (REPL
L3 25 S L1 (L) L2
L4 11 DUP REM L3 (14 DUPLICATES REMOVED)
L5 7 S L4 AND PY<=2000
E TRONO DID?/AU
L6 149 S E4
L7 2 S E5
L8 151 S L6 OR L7
L9 4 S L2 AND L8
L10 3 DUP REM L9 (1 DUPLICATE REMOVED)
L11 654 S (LENTIVIR? OR HIV(3W)VECTOR) (L) ((SELF(2W)INACTIVA?) OR (REP
L12 85 S L11 (L) L1
L13 36 DUP REM L12 (49 DUPLICATES REMOVED)
L14 11 S L11 AND L8
L15 10 DUP REM L14 (1 DUPLICATE REMOVED)
L16 10 FOCUS L15 1-

=> d an ti so au ab pi l16 1-6

L16 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:23440 CAPLUS
DN 138:84478
TI **Self-inactivating lentiviral** vectors for gene therapy capable of driving high level expression of therapeutic genes
SO U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
IN **Trono, Didier**; Salmon, Patrick
AB **HIV-derived lentivirus vectors** which are safe, highly efficient, and drive high levels of expression of transgenes in human cells for gene therapy, especially, in human hematopoietic progenitor cells as well as in all other blood cell derivs. are described. The **lentiviral** vectors comprise a **self-inactivating** configuration for biosafety. The vectors carry only the gag, pol, and rev genes. The promoter function of the long terminal repeats (LTR) is diminished by inactivation of the U3 region of the right LTR. Promoters such as the EF1α promoter are used to drive transgene expression and addnl. promoters are also described. The vectors can also comprise addnl. transcription enhancing elements such as the wood chuck hepatitis virus post-transcriptional regulatory element. These vectors therefore provide useful tools for genetic treatments such as inherited and acquired lympho-hematol. disorders, gene-therapies for cancers especially the hematol. cancers, as well as for the study of hematopoiesis via lentivector-mediated modification of human HSCs. Construction of vectors based on HIV-1 and murine leukemia virus is demonstrated. Vectors pseudotyped with vesicular stomatitis virus G glycoproteins efficiently infected CD34+ cells. Efficient expression of reporter genes from PGK and EF1α promoters was seen.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003008374	A1	20030109	US 2001-10081	20011109

L16 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:760311 CAPLUS
DN 130:120179
TI **Self-inactivating lentivirus** vector for safe and efficient in vivo gene delivery
SO Journal of Virology (1998), 72(12), 9873-9880
CODEN: JOVIAM; ISSN: 0022-538X
AU Zufferey, Romain; Dull, Thomas; Mandel, Ronald J.; Bukovsky, Anatoly; Quiroz, Dulce; Naldini, Luigi; **Trono, Didier**
AB In vivo transduction of nondividing cells by human immunodeficiency virus type 1 (HIV-1)-based **vectors** results in transgene expression that is stable over several months. However, the use of

HIV-1 vectors raises concerns about their safety. Here we describe a self-inactivating HIV-1 vector with a 400-nucleotide deletion in the 3' long terminal repeat (LTR). The deletion, which includes the TATA box, abolished the LTR promoter activity but die not affect vector titers or transgene expression in vitro. The self-inactivating vector transduced neurons in vivo as efficiently as a vector with full-length LTRs. The inactivation design achieved in this work improves significantly the biosafety of HIV-derived vectors, as it reduces the likelihood that replication-competent retroviruses will originate in the vector producer and target cells, and hampers recombination with wild-type HIV in an infected host. Moreover, it improves the potential performance of the vector by removing LTR sequences previously associated with transcriptional interference and suppression in vivo and by allowing the construction of more-stringent tissue-specific or regulatable vectors.

L16 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:117973 CAPLUS
DN 138:164686
TI Highly contained replication incompetent lentiviral gene therapy vectors and systems for their propagation
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
IN Trono, Didier; Zufferey, Romain N.
AB Lentivirus vectors derived from human immunodeficiency virus that have a number of modifications that make them very safe, efficient, high-level expression vectors for gene therapy are described. The modifications include, in combination: an inactive central polypurine tract, a stuffer sequence, which may encode drug susceptibility genes, and a mutated hairpin in the 5' leader sequence that substantially abolishes replication. In addition, genes essential for viral replication are on plasmids containing mutations that prevent replication competent virus being formed by recombination. These elements are provided in conjunction with other features of lentiviral vectors, such as a self-inactivating configuration for biosafety and promoters such as the EF1α promoter as one example. Addnl. promoters are also described. The vectors can also comprise addnl. transcription enhancing elements such as the wood chuck hepatitis virus post-transcriptional regulatory element. These vectors therefore provide useful tools for genetic treatments for inherited and acquired disorders, gene-therapies for cancers and other disease, the creation of industrial and exptl. production systems utilizing transformed cells, as well as for the study of basic cellular and genetic processes.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003012054	A2	20030213	WO 2002-US24275	20020801
WO 2003012054	A3	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003082789	A1	20030501	US 2002-209952	20020801
EP 1412493	A2	20040428	EP 2002-763401	20020801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

L16 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:52217 CAPLUS
DN 132:198941
TI Self-inactivating lentiviral vectors with enhanced transgene expression as potential gene transfer system in Parkinson's disease
SO Human Gene Therapy (2000), 11(1), 179-190

CODEN: HGTHE3; ISSN: 1043-0342

AU Deglon, Nicole; Tseng, Jack L.; Bensadoun, Jean-Charles; Zurn, Anne D.; Arsenijevic, Yvan; De Almeida, Luis Pereira; Zufferey, Romain; **Trono, Didier**; Aebischer, Patrick

AB Glial cell line-derived neurotrophic factor (GDNF) is able to protect dopaminergic neurons against various insults and constitutes therefore a promising candidate for the treatment of Parkinson's disease. **Lentiviral** vectors that infect quiescent neuronal cells may allow the localized delivery of GDNF, thus avoiding potential side effects related to the activation of other brain structures. To test this hypothesis in a setting ensuring both maximal biosafety and optimal transgene expression, a **self-inactivating** (SIN) **lentiviral** vector was modified by insertion of the posttranscriptional regulatory element of the woodchuck hepatitis virus, and particles were produced with a multiply attenuated packaging system. After a single injection of 2 μl of a lacZ-expressing vector (SIN-W-LacZ) in the substantia nigra of adult rats, an average of 40.1 ± 6.0% of the tyrosine hydroxylase (TH)-pos. neurons were transduced as compared with 5.0 ± 2.1% with the first-generation **lentiviral** vector. Moreover, the SIN-W vector expressing GDNF under the control of the mouse phosphoglycerate kinase 1 (PGK) promoter was able to protect nigral dopaminergic neurons after medial forebrain bundle axotomy. Expression of hGDNF in the nanogram range was detected in exts. of mesencephalon of animals injected with an SIN-W-PGK-GDNF vector, whereas it was undetectable in animals injected with a control vector. **Lentiviral** vectors with enhanced expression and safety features further establish the potential use of these vectors for the local delivery of bioactive mols. into defined structures of the central nervous system.

L16 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:632319 CAPLUS

DN 125:266887

TI Efficient transfer, integration, and sustained long-term expression of the transgene in adult rat brains injected with a lentiviral vector

SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(21), 11382-11388
CODEN: PNASA6; ISSN: 0027-8424

AU Naldini, Luigi; Blomer, Ulrike; Gage, Fred H.; **Trono, Didier**; Verma, Inder M.

AB We describe the construction of a safe, replication-**defective** and efficient **lentiviral** vector suitable for in vivo gene delivery. The reverse transcription of the vector was found to be a rate-limiting step; therefore, promoting the reaction inside the vector particles before delivery significantly enhanced the efficiency of gene transfer. After injection into the brain of adult rats, sustained long-term expression of the transgene was obtained in the absence of detectable pathol. A high proportion of the neurons in the areas surrounding the injection sites of the vector expressed the transduced β-galactosidase gene. This pattern was invariant in animals sacrificed several months after a single administration of the vector. Transduction occurs by integration of the vector genome, as it was abolished by a single amino acid substitution in the catalytic site of the integrase protein incorporated in the vector. Development of clin. acceptable derivs. of the **lentiviral** vector may thus enable the sustained delivery of significant amts. of a therapeutic gene product in a wide variety of somatic tissues.

L16 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:816778 CAPLUS

DN 135:14992

TI High-level transgene expression in human hematopoietic progenitors and differentiated blood lineages after transduction with improved lentiviral vectors

SO Blood (2000), 96(10), 3392-3398
CODEN: BLOOAW; ISSN: 0006-4971

AU Salmon, Patrick; Kindler, Vincent; Ducrey, Odile; Chapuis, Bernard; Zubler, Rudolf H.; **Trono, Didier**

AB Recent expts. point to the great value of **lentiviral** vectors for the transduction of human hematopoietic stem cells (hHSCs). Vectors used

so far, however, have been poorly satisfying in terms of either biosafety or efficiency of transgene expression. Herein is described the results obtained with human immunodeficiency virus-based vectors optimized in both of these aspects. It is thus shown that vectors containing the EF1α and, to a lesser extent, the phosphoglycerate kinase (PGK) promoter, govern high-level gene expression in human hematopoietic progenitors as well as derived hematopoietic lineages of therapeutic relevance, such as erythrocytes, granulocytes, monocytes, dendritic cells, and megakaryocytes. EF1α promoter-containing **lentiviral** vectors can also induce strong transgene expression in primary T lymphocytes isolated from peripheral blood. A **self-inactivating** design did not affect the performance of EF1α promoter-based vectors but significantly reduced expression from the PGK promoter. This neg. effect could nevertheless be largely rescued by inserting the post-transcriptional regulatory element of woodchuck hepatitis virus upstream of the vector 3' long terminal repeat. These results have important practical implications for the genetic treatment of lymphohematol. disorders as well as for the study of hematopoiesis via the lentivector-mediated modification of hHSCs.